

A phylogenetic confidence interval for the optimal trait value

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Abstract

We consider a model for adaptive evolution of a phenotype within a family of related species with unknown phylogeny. The unknown species tree is modelled by a Yule process conditioned on having n tips. The trait value is assumed to evolve along a lineage as an Ornstein–Uhlenbeck process characterized by the adaptation rate $\alpha > 0$, the optimal trait value θ and the noise size $\sigma > 0$. For the vector of n trait values describing the outcome of such an evolution we study the moments of the sample mean and sample variance. Our analytical and simulation results lead to a simple confidence interval for θ when α is larger than half the speciation rate.

Keywords : Phylogenetic comparative methods, Conditioned Yule branching process, Branching Ornstein–Uhlenbeck process, Phylogenetic confidence intervals, Phylogenetic tree metric

1 Introduction

Phylogenetic comparative methods are by now well established and provide important tools for studying interspecies data. In short they provide a methodology to take into account the evolutionary relationships between observed species when studying their traits and potential relationships with the environment the species live in. Assuming a stochastic process under which the phenotype evolves on the tree, it is desirable to estimate the process' parameters and appropriately interpret them. As with any statistical procedure it is important to place confidence

intervals around the point estimates for the parameters of interest. However, confidence intervals are often not mentioned in the phylogenetic comparative methods literature as pointed out by Boettiger et al. (2012).

There are a number of possible ways of calculating these confidence intervals and very often they may take intolerable amounts of time depending on the assumed stochastic model of evolution. If the tree is known and the estimation procedure can be put in a regression framework, then standard regression type confidence intervals may be used (e.g. Hansen, 1997; Martins and Hansen, 1997; Garland and Ives, 2000; Rohlf, 2001). In more complicated situations a parametric bootstrap is a way out (Boettiger et al., 2012), used by e.g. Ives et al. (2007) and implemented in the *ouch* package (Butler and King, 2004). Another approach is to consider the curvature of the likelihood surface (done by e.g. Bartoszek et al., in revision) in situations where a parametric bootstrap is too time consuming. In parametric settings with only few parameters involved, reporting a support region (Hansen, 1997; Hansen et al., 2008) is a significantly more attractive option.

All of the above methods have in common that they assume that the phylogeny describing the evolutionary relationships is fully resolved. Possible errors in the topology can cause problems – the closer to the tips they occur, the more problematic they can be (Symonds, 2002). Practically, in view of the wealth of sequence information and the advancement in phylogeny reconstruction techniques, the assumption of a completely resolved species tree is justifiable. Also from a statistical point of view this might not be at first glance such a large problem as regression estimators will remain unbiased even with a misspecified tree (Rohlf, 2006), and also seem to be robust with respect to errors in phylogeny (at least for the Brownian motion model of phenotype evolution, as noticed by Stone, 2011).

A direction of study which seems to be underrepresented currently is connecting phylogenetic comparative methods, in particular their underlying stochastic models of evolution, with stochastic models of tree growth. There are of course exceptions to this, e.g., already in the 1970s, a joint maximum likelihood estimation procedure of a Yule tree and Brownian motion on top of it was proposed by Edwards (1970), and an MCMC procedure to jointly estimate the phylogeny and parameters of the Brownian model of trait evolution has been proposed by Huelsenbeck et al. (2000); Huelsenbeck and Rannala (2003).

Assuming a stochastic model for the tree's growth allows one to study the properties of a sample of species without the need to use a fixed phylogeny. From the point of view of a comparative analysis this can be useful in a number of situations: if the phylogenetic tree is known to be poorly resolved, or if one wants to see how robust the results are with respect to uncertainty in the phylogeny. The case

of unresolved trees can appear e.g. when studying fossil data. There may be available rich phenotypic information but the molecular material might have degraded so much that it is impossible to infer evolutionary relationships. “Integrating” over the phylogeny can be used as a sanity check, whether the conclusions based on the inferred phylogeny deviate much from those from a “typical” phylogeny. Results presented here can also be used as a method of testing software for phylogenetic comparative models.

In this work we propose a simple phylogenetic confidence interval formula which takes into account the phylogenetic uncertainty. To this end we study properties of the sample mean and sample variance

$$\bar{X}_n = \frac{X_1 + \dots + X_n}{n}, \quad S_n^2 = \frac{1}{n-1} \sum_{i=1}^n (X_i - \bar{X}_n)^2,$$

for the vector of trait values (X_1, \dots, X_n) in the framework of what we call the Yule–Ornstein–Uhlenbeck (YOU) model. The YOU–model is characterized by four parameters $(X_0, \alpha, \sigma, \theta)$ and consists of two ingredients

1. the species tree connecting n extant species is modeled by the pure birth Yule process (Yule, 1924) with a unit speciation rate $\lambda = 1$ and conditioned on having n tips,
2. the observed values (X_1, \dots, X_n) evolved from the ancestral state X_0 following the Ornstein–Uhlenbeck (OU) process with parameters (α, σ, θ) .

The conditioned Yule tree (Gernhard, 2008a) has a convenient backward description in terms of n inter–speciation times $(T_n, T_{n-1}, \dots, T_1)$ which are independent exponential random variables with parameters $(n, n-1, \dots, 1)$. Here T_k is the time during which the tree has k branches, so that

$$T = T_1 + \dots + T_n \tag{1}$$

is the total height of the tree and the ancestral trait value X_0 is attributed to the corresponding time which we call time to the origin, see Fig. 1. For more details on treating such combinations of exponential random variables the reader is referred to Feller (1966), Yule trees are discussed by e.g. Athreya and Ney (2000) and a consideration of applications of branching processes in biology is presented by e.g. Haccou et al. (2007).

The OU–process $X(t)$ described by the stochastic differential equation

$$dX(t) = -\alpha(X(t) - \theta)dt + \sigma dB(t), \quad X(0) = X_0, \tag{2}$$

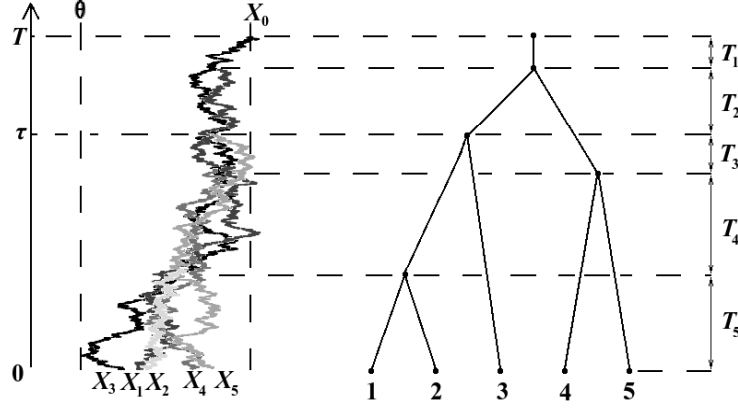


Figure 1: On the left: a branching OU-process simulated on a random tree with $n = 5$ tips using the TreeSim (Stadler, 2009, 2011) and mvSLOUCH (Bartoszek et al., in revision) software. Parameters used are $\alpha = 1$, $\sigma = 1$, $X_0 - \theta = 2$, after the tree height T was scaled to 1. On the right: the species tree disregarding the trait values supplied with the notation for the inter-speciation times. For the pair of tips (2,3) the time τ to their most recent common ancestor is marked on the time axis (starting at present and going back to the time of origin).

can be interpreted (Hansen, 1997; Butler and King, 2004; Hansen and Orzack, 2005; Hansen et al., 2008; Labra et al., 2009) as the evolution of a trait value along a lineage of species in terms of the adaptation rate $\alpha > 0$, the optimal trait value θ , and the noise size $\sigma > 0$. The distribution of $X(t)$ is normal with

$$E[X(t)] = \theta + e^{-\alpha t}(X_0 - \theta), \quad \text{Var}[X(t)] = \sigma^2(1 - e^{-2\alpha t})/2\alpha \quad (3)$$

implying that $X(t)$ loses the effect of the ancestral state X_0 at an exponential rate. In the long run the OU-process acquires a stationary normal distribution with mean θ and variance $\sigma^2/2\alpha$. Notice that with $\alpha = 0$ there is no adaptation and the trait evolution is governed by the Brownian motion (Felsenstein, 1985).

Using these properties of the YOU-model we find explicit expressions for $E[\bar{X}_n]$, $\text{Var}[\bar{X}_n]$, and $E[S_n^2]$ and propose a simple formula for an asymptotic phylogenetic confidence interval for the optimal value θ as presented in Section 2 and supported by simulations, see Section 3. Our confidence interval formula Eq. (11) is meant to incorporate not only the randomness in the trait evolution but also the uncertainty in the species tree. Even if we have a resolved tree using such an interval estimate allows one to see how much worse would one do, if there was

any potential error in the tree. Based on this one can decide whether a detailed recheck of phenotypic conclusions with respect to variations in the phylogeny is necessary or not.

In Sections 4 and 5 we give the proofs of our main results summarized in Section 2. Section 5 contains new formulae for the Laplace transforms for the important characteristics of the conditioned Yule species tree: the time to origin T and the time τ to the most recent common ancestor for a pair of two species chosen at random out of n extant species.

Section 6 gives exact formulae for the first two moments for T and τ which are applied to compute the mean of the squared splitted nodal distance between two independent realizations of the conditioned Yule model. Finally, in Section 7 we give recursive formulae for all moments of T and τ as well as all joint moments of $T - \tau$ and τ .

2 Summary of main results

In the framework of the YOU-model with parameters $(X_0, \alpha, \theta, \sigma)$ the random variables \bar{X}_n and $E[S_n^2]$ have two sources of uncertainty: unknown species tree and stochastic trait evolution along the branches of the tree. In this section we present exact and approximate expressions for $E[\bar{X}_n]$, $\text{Var}[\bar{X}_n]$, and $E[S_n^2]$. It is important to recognize that our standing assumption $\lambda = 1$ of having one speciation event per unit of time causes no loss of generality. To incorporate an arbitrary speciation rate λ one has to replace in our formulae parameters α and σ^2 by $\hat{\alpha} = \alpha/\lambda$ and $\hat{\sigma}^2 = \sigma^2/\lambda$. This transformation, in view of Eq. (2), is equivalent to a time scaling by factor λ : if $t = \hat{t}/\lambda$, then $\alpha dt = \hat{\alpha} d\hat{t}$ and $\sigma dB(t) = \hat{\sigma} dB(\hat{t})$. This transformation changes neither the optimal value θ nor the stationary variance $\sigma^2/(2\alpha)$.

Under the YOU-model we show that

$$E[\bar{X}_n] = b_{n,\alpha} X_0 + (1 - b_{n,\alpha}) \theta, \quad (4)$$

where

$$b_{n,x} = \frac{1}{1+x} \cdot \frac{2}{2+x} \cdots \frac{n}{n+x}. \quad (5)$$

We see that the sample mean \bar{X}_n is an unbiased estimator of

- the ancestral state X_0 in the Brownian motion case, $\alpha = 0$, since $b_{n,0} = 1$,
- a weighted mean of the ancestral trait value and the optimal value when $0 < \alpha < \infty$ which asymptotically, as the sample size increases, becomes the optimal value.

Note that even for moderate values of α the weighted mean Eq. (4) is close to θ . For example, with $\alpha = 1$ we get $E[\bar{X}_n] = \frac{1}{n+1}X_0 + \frac{n}{n+1}\theta$.

Secondly, we find that

$$\text{Var}[\bar{X}_n] = \frac{\sigma^2}{2\alpha} \cdot \frac{2\alpha + 1 - (4\alpha n + 2\alpha + 1)b_{n,2\alpha}}{(2\alpha - 1)n} + (X_0 - \theta)^2(b_{n,2\alpha} - b_{n,\alpha}^2). \quad (6)$$

In the singular case $\alpha = 1/2$ Eq. (6) reads

$$\text{Var}[\bar{X}_n] = \frac{\sigma^2}{n} \left(2a_n - \frac{3n}{n+1} \right) + (X_0 - \theta)^2(b_{n,1} - b_{n,0.5}^2),$$

where $a_n = 1 + 1/2 + \dots + 1/n$ is the n -th harmonic number. The last expression is obtained from Eq. (6) by applying the asymptotic formula

$$\frac{1 - (n+1)b_{n,x}}{x-1} \rightarrow a_{n+1} - 1, \quad x \rightarrow 1.$$

Notice that as $\alpha \rightarrow 0$, using the fact that

$$x^{-1}(1 - b_{n,x}) \rightarrow a_n, \quad x \rightarrow 0,$$

we recover from Eq. (6) the formula for the Brownian motion model

$$\text{Var}[\bar{X}_n] = \sigma^2 \left(2 - \frac{a_n}{n} \right), \quad (7)$$

obtained earlier by Sagitov and Bartoszek (2012).

Letting $n \rightarrow \infty$ in Eq. (6) and using

$$\frac{b_{n,x}}{\Gamma(x+1)} = \frac{\Gamma(n+1)}{\Gamma(n+x+1)} \sim n^{-x}$$

we get a wide range of asymptotic regimes:

$$\text{Var}[\bar{X}_n] \sim \sigma^2 \cdot \begin{cases} 2, & \text{if } \alpha = 0, \\ C_{\alpha,\delta} \cdot n^{-2\alpha}, & \text{if } 0 < \alpha < 0.5, \\ 2n^{-1} \ln n, & \text{if } \alpha = 0.5, \\ \frac{2\alpha+1}{2\alpha(2\alpha-1)n}, & \text{if } \alpha > 0.5, \end{cases} \quad (8)$$

where $\delta = \frac{|X_0 - \theta|}{\sigma}$ is the normalized distance between the ancestral and optimal values and

$$C_{x,\delta} = \frac{2}{1-2x} \Gamma(2x+1) + 2\alpha\delta^2 \Gamma(2x+1) - 2\alpha\delta^2 \Gamma^2(x+1).$$

Thirdly, we compute

$$\mathbb{E}[S_n^2] = \frac{\sigma^2}{2\alpha} \left(1 + \frac{(2\alpha + 1)(n + 1)b_{n,2\alpha} - 2}{(2\alpha - 1)(n - 1)} \right), \quad (9)$$

which in the case $\alpha = 0.5$ turns into

$$\mathbb{E}[S_n^2] = \sigma^2 \left(1 - \frac{2a_{n+1} - 3}{n - 1} \right).$$

Letting $\alpha \rightarrow 0$ in Eq. (9) we arrive at the formula obtained by Sagitov and Bartoszek (2012) for the Brownian motion model

$$\mathbb{E}[S_n^2] = \sigma^2 \left(\frac{n + 1}{n - 1} a_n - \frac{2n}{n - 1} \right). \quad (10)$$

Observe that for any fixed $\alpha > 0$ we have,

$$\begin{aligned} \mathbb{E}[\bar{X}_n] &= \theta + O(\delta n^{-\alpha}), \\ \mathbb{E}[S_n^2] &\xrightarrow{n \rightarrow \infty} \frac{\sigma^2}{2\alpha}, \end{aligned}$$

making \bar{X}_n and S_n^2 asymptotically unbiased estimators of the optimal state θ and the stationary variance of the OU process respectively. This is in accordance with the finding of Hansen (1997) where in a regression setup the residual sum of squares was used to estimate the stationary variance. Additionally in the case of sufficiently strong adaptation when $\alpha > 0.5$ letting $n \rightarrow \infty$, we have

$$\text{Var}[\bar{X}_n] \sim \frac{2\alpha + 1}{2\alpha(2\alpha - 1)} \cdot \frac{\sigma^2}{n}.$$

Taking the last relation into account, when $\alpha > 0.5$, we propose the following convenient approximate formula for a 95% confidence interval for the optimal trait value θ :

$$\bar{X}_n \pm 1.96 \cdot S_n \cdot \frac{K_\alpha}{\sqrt{n}}, \quad K_\alpha = \sqrt{\frac{2\alpha + 1}{2\alpha - 1}}, \quad \alpha > 0.5. \quad (11)$$

The confidence interval from Eq. (11) differs from the classical confidence interval for the mean ($\bar{X}_n \pm 1.96S_n/\sqrt{n}$) just by a factor K_α . The latter is larger than 1, as it should, in view of a positive correlation among the sample observations. The correction factor K_α becomes negligible in the case of a very strong adaptation, $\alpha \gg 1$, when the dependence due to common ancestry can be neglected.

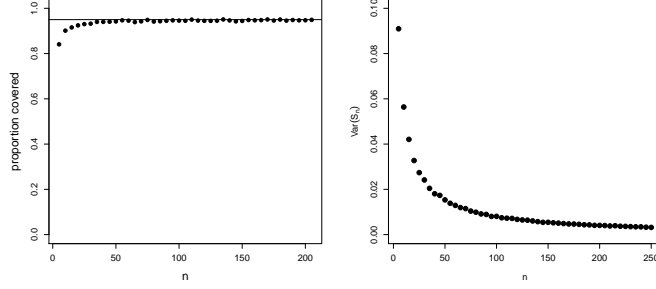


Figure 2: Simulation results supporting the confidence interval formula Eq. (11). Simulations are performed for the YOU-model with $\lambda = 1$, $\alpha = 1$, $\sigma = 1$, $X_0 = 1$, $\theta = 0$. Left: each dot gives the proportion of the 10000 confidence intervals covering θ for a particular value of n . The horizontal line is the desired 95% coverage level. Right: the simulation results for $\text{Var}[S_n^2]$ decrease toward zero with n suggesting that S_n^2 is a consistent estimator of the stationary variance.

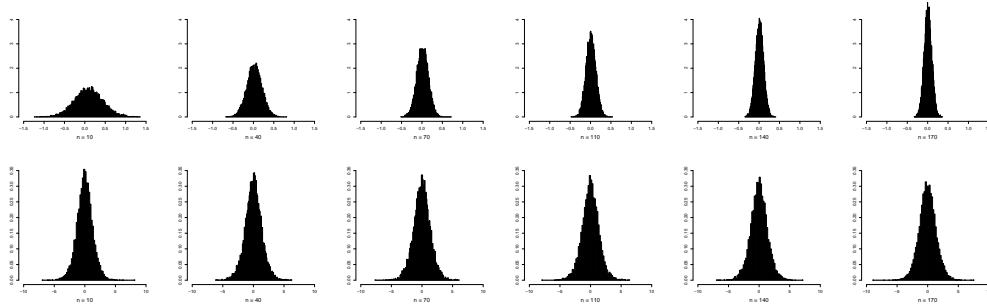


Figure 3: Top row: histograms of \bar{X}_n for the Ornstein-Uhlenbeck model for different value of n (left to right: 10, 40, 70, 110, 140, 170), for each 10000 independent values of \bar{X}_n were simulated. In the simulations $\alpha = 1$, $X_0 = 1$, $\theta = 0$ and $\sigma^2 = 1$. For all histograms the x and y axes have the same scale $x \in (-1.5, 1.5)$, $y \in (0, 4)$. Bottom row: histograms of \bar{X}_n for the Brownian motion model with the same values of n as on the top row. In the simulations $X_0 = 0$ and $\sigma^2 = 1$, the axes values here are in the range $x \in (-10, 10)$ and $y \in (0, 0.35)$.

3 Phylogenetic confidence intervals

Our confidence interval formula Eq. (11) is well supported by simulation results presented in Fig. 2. A strict mathematical justification of this formula hinges on two results which need to be addressed in a future study as they depend on properties of conditioned Yule trees that require further work. One has to prove that

$$\text{Var}[S_n^2] \rightarrow 0, \quad n \rightarrow \infty \quad (12)$$

and the following central limit theorem has to be verified,

Conjecture 3.1 *As $n \rightarrow \infty$, the standardized sample mean*

$$Z_n = (\bar{X}_n - \text{E}[\bar{X}_n])(\text{Var}[\bar{X}_n])^{-1/2} \quad (13)$$

is asymptotically normally distributed with parameters (0,1).

We performed extensive simulations finding support for Eq. (12), see the right panel in Fig. 2, and our conjecture of asymptotic normality for Z_n . The bell-shaped histograms in the first row of Fig. 3 illustrate the decrease of the variance predicted by the theory, see the left panel in Fig. 4. As shown on the central panel in Fig. 4, the Shapiro–Wilk test does not indicate significant deviations from normality, and moreover, the estimate of the excess kurtosis (not shown) oscillates around 0 for large n .

A more thorough check of normality for Eq. (13) is given by a hybrid Monte–Carlo–numerical approach described below in Algorithm 1. The key idea behind Algorithm 1 is that conditional on the species tree \bar{X}_n is normally distributed. Our R (R Development Core Team, 2010) implementation of this algorithm is available on request. The right panel in Fig. 4 demonstrates that with increasing n the 0.975–quantile of the distribution of Z_n approaches the 0.975–quantile of the standard normal distribution.

Another example of a phylogenetic confidence interval can be suggested in the case of the Brownian motion model of evolution where the sample average is an unbiased estimator of the ancestral state X_0 . Using Eq. (7) and assuming σ is known one can think of the following approximate 95% confidence interval for X_0

$$\bar{X}_n \pm q_n \frac{\sigma}{\sqrt{n}} \sqrt{2n - a_n}, \quad (14)$$

whose symmetric form is justified by histograms in the second row of Fig. 3. From Fig. 5 we can see that the appropriate value of q_n should lie somewhere

Algorithm 1 Find approximate $1 - \alpha (= 0.975$ in our case) level quantile of \bar{X}_n

- 1: Simulate $N (= 10000$ in our case) trees with n tips and specified birth–death rates using TreeSim (Stadler, 2009, 2011).
- 2: Conditioned on the tree i calculate the mean (μ_i) and variance (σ_i^2) of \bar{X}_n under the desired stochastic process of phenotype evolution.
- 3: Calculate the unconditional $E[\bar{X}_n]$ and $\text{Var}[\bar{X}_n]$ under the assumed stochastic models of tree growth and phenotype evolution.
- 4: Use the R function `optim()` to minimize,

$$\left((1 - \alpha) - \frac{1}{N} \sum_{i=1}^N \Phi \left(\frac{E[\bar{X}_n] + q\sqrt{\text{Var}[\bar{X}_n]} - \mu_i}{\sigma_i} \right) \right)^2$$

with respect to q , where $\Phi(\cdot, \mu, \sigma^2)$ is the cumulative distribution function for a normal distribution with mean μ and variance σ^2 .

between the normal and t distribution quantiles. Obviously the width of the confidence interval of Eq. (14) does not converge to zero as $n \rightarrow \infty$ (also observed by Ané, 2008, but with a different model of tree growth). The kurtosis estimates and Shapiro–Wilk test p-values indicate that the distribution of \bar{X}_n deviates from normality and this should be remembered when applying them to data, see Fig. 5. On the other hand, the histograms in Fig. 4 do not indicate that a practitioner should be overly worried about this.

4 Derivation of key formulae

In this section we derive Eqs. (4), (6) and (9). Let X and Y be a pair of trait values randomly chosen (without replacement) from n available values (X_1, \dots, X_n) . Denote by τ the time until the most recent common ancestor for the pair of species behind the sampled trait values X and Y . Using conditioning on the time of origin T and Eq. (3) we obtain

$$E[X] = E[E[X|T]] = E[\theta + e^{-\alpha T}(X_0 - \theta)] = \theta + (X_0 - \theta)E[e^{-\alpha T}], \quad (15)$$

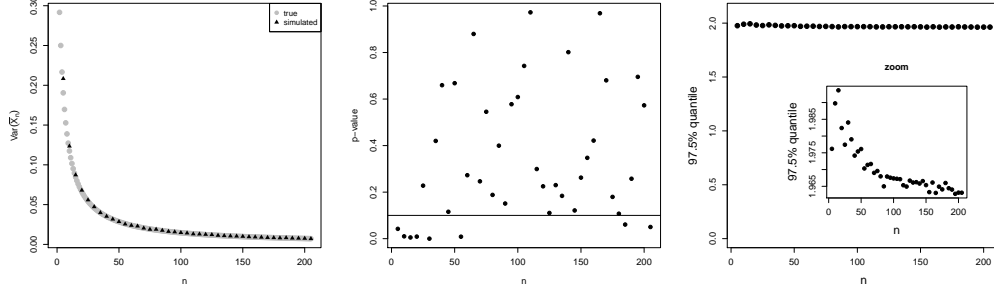


Figure 4: Simulation results concerning \bar{X}_n for the YOU-model with $\alpha = 1$, $X_0 = 1$, $\theta = 0$, $\sigma^2 = 1$. Left: variance of the sample mean, simulated and theoretical values as functions of n . Center: p-value of Shapiro–Wilk test for normality (Royston, 1995, indicates 0.1 as an adequate cut-off level). Right: 0.975 level quantile calculated according to Algorithm 1 (the inset in the graph is a zoom-in on the y-axis around the points). Each point is estimated from 10000 Yule trees, except for the Shapiro–Wilk test, where a subsample of 5000 trees was used due to the requirements of the `shapiro.test()` R function.

and

$$\begin{aligned}
 \text{Var}[X] &= \text{E}[\text{Var}[X|T]] + \text{Var}[\text{E}[X|T]] \\
 &= \text{E}\left[\frac{\sigma^2}{2\alpha}(1 - e^{-2\alpha T})\right] + \text{Var}[(X_0 - \theta)e^{-\alpha T} + \theta] \\
 &= \frac{\sigma^2}{2\alpha}(1 - \text{E}[e^{-2\alpha T}]) + (X_0 - \theta)^2 \text{Var}[e^{-\alpha T}].
 \end{aligned} \tag{16}$$

Since obviously $\text{E}[\bar{X}_n] = \text{E}[X]$, Eq. (15) yields

$$\text{E}[\bar{X}_n] = \theta + (X_0 - \theta)\text{E}[e^{-\alpha T}]. \tag{17}$$

Next, conditioning on τ and the trait value X_τ of the most recent common ancestor of the randomly chosen pair of extant species, we get by applying Eq. (3)

$$\begin{aligned}
 \text{Cov}[X, Y] &= \text{E}[\text{Cov}[X, Y|\tau, X_\tau]] + \text{Cov}[\text{E}[X|\tau, X_\tau], \text{E}[Y|\tau, X_\tau]] \\
 &= \text{Var}[(X_\tau - \theta)e^{-\alpha\tau} + \theta].
 \end{aligned}$$

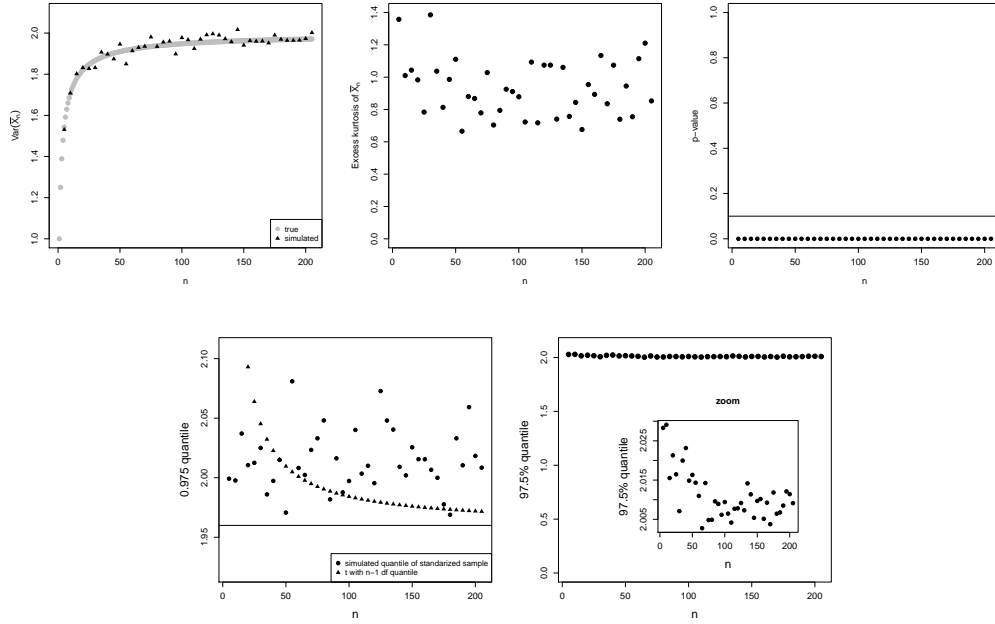


Figure 5: Characteristics of the distribution of \bar{X}_n for the Brownian motion model with $X_0 = 0$ and $\sigma^2 = 1$. Top left: variance of \bar{X}_n , top centre: excess kurtosis estimate for standardized \bar{X}_n , top right: p-value of Shapiro–Wilk test for normality, bottom left: 0.975–quantiles of standardized \bar{X}_n , bottom right: 0.975–quantile calculated according to Algorithm 1. Each point is estimated from 10000 independently simulated Yule trees, except for the Shapiro–Wilk test based on 5000 trees.

Conditioning on (T, τ) gives

$$\begin{aligned}\text{Var}[(X_\tau - \theta)e^{-\alpha\tau}] &= \text{E}[e^{-2\alpha\tau} \text{Var}[X_\tau|T, \tau]] + \text{Var}[e^{-\alpha\tau} \text{E}[X_\tau - \theta|T, \tau]] \\ &= \text{E}\left[e^{-2\alpha\tau} \frac{\sigma^2}{2\alpha}(1 - e^{-2\alpha(T-\tau)})\right] + \text{Var}\left[e^{-\alpha\tau}(X_0 - \theta)e^{-\alpha(T-\tau)}\right].\end{aligned}$$

Therefore it follows that

$$\text{Cov}[X, Y] = \frac{\sigma^2}{2\alpha}(\text{E}[e^{-2\alpha\tau}] - \text{E}[e^{-2\alpha T}]) + (X_0 - \theta)^2 \text{Var}[e^{-\alpha T}]. \quad (18)$$

It was shown by Sagitov and Bartoszek (2012) that the variance of the sample average and the expectation of the sample variance can be compactly expressed

$$\text{Var}[\bar{X}_n] = \text{Var}[X] - \frac{n-1}{n}(1 - \rho_n) \text{Var}[X], \quad (19)$$

$$\text{E}[S_n^2] = (1 - \rho_n) \text{Var}[X] \quad (20)$$

in terms of the interspecies correlation coefficient $\rho_n = \text{Cov}[X, Y] / \text{Var}[X]$, first studied by Sagitov and Bartoszek (2012) for the Brownian motion model. In view of Eqs. (16) and (18), for the YOU-model the interspecies correlation takes the form

$$\rho_n = 1 - \frac{\frac{\sigma^2}{2\alpha}(1 - \text{E}[e^{-2\alpha\tau}])}{\frac{\sigma^2}{2\alpha}(1 - \text{E}[e^{-2\alpha T}]) + (X_0 - \theta)^2 \text{Var}[e^{-\alpha T}]}. \quad (21)$$

Putting together Eqs. (16), (19), (20), and (21) we arrive at

$$\begin{aligned}\text{Var}[\bar{X}_n] &= \frac{\sigma^2}{2\alpha n} (1 - n\text{E}[e^{-2\alpha T}] + (n-1)\text{E}[e^{-2\alpha\tau}]) + (X_0 - \theta)^2 \text{Var}[e^{-\alpha T}], \\ \text{E}[S_n^2] &= \frac{\sigma^2}{2\alpha} (1 - \text{E}[e^{-2\alpha\tau}]).\end{aligned}$$

Eqs. (4), (6), (9) readily follow from Eq. (17) and the last two relations in view of

$$\text{E}[e^{-xT}] = b_{n,x}, \quad (22)$$

and

$$\text{E}[e^{-y\tau}] = \frac{2 - (n+1)(y+1)b_{n,y}}{(n-1)(y-1)}, \quad (23)$$

both derived in the next section. Note that Eq. (23) with $y = 1$ reads as

$$\text{E}[e^{-\tau}] = \frac{2}{n-1}(a_n - 1) - \frac{1}{n+1},$$

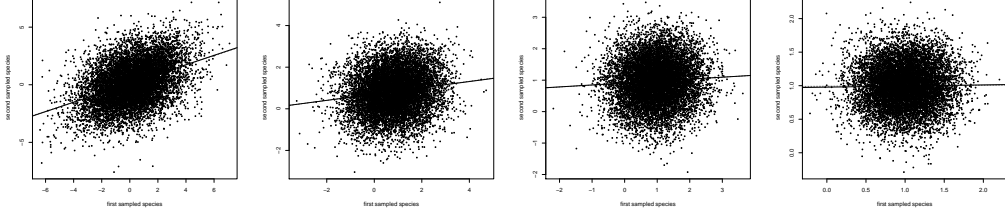


Figure 6: Simulation results in the case $\lambda = 1$, $\sigma^2 = 1$, $X_0 = 0$, $\theta = 1$, and $n = 30$. Regression lines fitted to simulated data (thick line) are indistinguishable from the true regression line $y = \rho_{30}x + (1 - b_{30,\alpha})(1 - \rho_{30})$, where ρ_{30} is given by Eqs. (24) and (25) for different values of α . From the left to the right: $\alpha = 0.05, 0.5, 1, 5$.

and that Eq. (23) entails

$$\text{Var}[e^{-\alpha T}] = b_{n,2\alpha} - b_{n,\alpha}^2.$$

We conclude this section by recording the exact formula of the interspecies correlation coefficient for the YOU-model in the case of $\alpha \neq 0.5$

$$\rho_n = 1 - \frac{2\alpha(n-1) + (n+1)((2\alpha+1)b_{n,2\alpha} - 1)}{(n-1)(2\alpha-1)(1 + (2\alpha\delta^2 - 1)b_{n,2\alpha} - 2\alpha\delta^2 b_{n,\alpha}^2)}, \quad (24)$$

and in the case of $\alpha = 0.5$,

$$\rho_n = 1 - \frac{n+1}{n-1} \frac{n+2-2a_{n+1}}{n + \delta^2(1 - (n+1)b_{n,0.5}^2)}, \quad (25)$$

where $\delta = \frac{|X_0 - \theta|}{\sigma}$. This formula, illustrated by Fig. 4, should be compared to similar formulae due to Sagitov and Bartoszek (2012) obtained for $\alpha = 0$ when the unknown species tree is modelled by a generalization of the conditioned Yule process, a conditioned birth–death process allowing for extinction of species.

5 Laplace transform for (T, τ)

The conditioned birth–death processes as stochastic models for species trees, have received significant attention in the last decade (e.g. Aldous and Popovic, 2005;

Gernhard, 2008a; Stadler, 2009, 2011; Mooers et al., 2012; Stadler and Steel, 2012). Here we contribute to these studies by computing the joint Laplace transform of, T , the height of a Yule tree conditioned on n tips at present and τ , the height of the most recent common ancestor for two randomly sampled tips (for results concerning the distribution of τ and T see also Gernhard, 2008a,b; Stadler, 2009). Figure 1 visualizes these random variables. This also allows us to give recursive formulae for the joint moments of T and τ .

Recall that we consider the Yule process with a unit speciation rate $\lambda = 1$. It is easy to extend the result below to the case of an arbitrary speciation rate λ : simply replace the times T and τ by $\hat{T} = T\lambda$ and $\hat{\tau} = \tau\lambda$.

Lemma 5.1 *Let κ_n ($1 \leq \kappa_n \leq n-1$) be the number of the splits in the tree (counted forward in time) corresponding to the coalescent of two randomly sampled tips. Then*

$$P(\kappa_n = k) = \frac{2(n+1)}{(n-1)(k+2)(k+1)}, \quad k = 1, \dots, n-1. \quad (26)$$

It follows that for any positive x and y we have

$$E \left[e^{-x(T-\tau)-y\tau} \right] = \frac{2(n+1)b_{n,y}}{(n-1)} \sum_{k=1}^{n-1} \frac{b_{k,x}}{(k+2)(k+1)b_{k,y}}, \quad (27)$$

implying Eqs. (22) and (23).

PROOF Tracing the lineages of two randomly sampled tips of the Yule tree towards the root, the coalescent can be viewed as the success in a sequence of independent Bernoulli trials. This argument leads to the expression

$$P(\kappa_n = k) = \left(1 - \frac{1}{\binom{n}{2}}\right) \cdot \dots \cdot \left(1 - \frac{1}{\binom{k+2}{2}}\right) \frac{1}{\binom{k+1}{2}}$$

yielding Eq. (26) after expanding the binomial coefficients. Eq. (27) follows easily from Eq. (5) and

$$E \left[e^{-x(T-\tau)-y\tau} \right] = \sum_{k=1}^{n-1} P(\kappa_n = k) \frac{1}{x+1} \cdot \dots \cdot \frac{k}{x+k} \frac{k+1}{y+k+1} \cdot \dots \cdot \frac{n}{y+n},$$

which is a consequence of the representation, in Eq. (1),

$$T - \tau = T_1 + \dots + T_{\kappa_n}, \quad \tau = T_{\kappa_n+1} + \dots + T_n.$$

Putting $y = x$ in Eq. (27) we obtain Eq. (22). Plugging $x = 0$ in Eq. (27) we get

$$\begin{aligned} \mathbb{E}[e^{-y\tau}] &= \frac{n+1}{n-1} \sum_{k=1}^{n-1} \frac{1}{\binom{k+2}{2}} \frac{k+1}{y+k+1} \cdot \dots \cdot \frac{n}{y+n} \\ &= \frac{2(n+1)!}{(n-1)\Gamma(y+n+1)} \sum_{k=1}^{n-1} \frac{\Gamma(k+1+y)}{\Gamma(k+3)}. \end{aligned}$$

When $y = 1$ this directly becomes,

$$\mathbb{E}[e^{-\tau}] = \frac{2}{n-1}(a_n - 1) - \frac{1}{n+1}$$

and for $y \neq 1$ we use the following relation (easily verified by induction when $z \neq y$)

$$\sum_{k=1}^{n-1} \frac{\Gamma(k+y)}{\Gamma(k+z+1)} = \frac{\Gamma(n+z)\Gamma(y+1) - \Gamma(z+1)\Gamma(n+y)}{\Gamma(z+1)\Gamma(n+z)(z-y)} \quad (28)$$

to derive Eq. (23)

$$\mathbb{E}[e^{-y\tau}] = \frac{2\Gamma(n+1+y) - \Gamma(n+2)\Gamma(y+2)}{(n-1)\Gamma(y+n+1)(y-1)} = \frac{2 - (n+1)(y+1)b_{n,y}}{(n-1)(y-1)}.$$

□

6 First two moments of T and τ

In Section 7 using Eq. (27) we present a recursive procedure for obtaining all the joint moments of T and τ . In particular, the first two moments are

$$\begin{aligned} \mathbb{E}[T] &= a_n, \quad \mathbb{E}[T^2] = a_n^2 + H_{n,2}, \\ \mathbb{E}[\tau] &= \frac{n+1}{n-1}a_n - \frac{2n}{n-1}, \quad \mathbb{E}[\tau^2] = \frac{n+1}{n-1}(a_n^2 + H_{n,2}) - \frac{4(a_n(n+1) - n)}{n-1}, \\ \mathbb{E}[T\tau] &= \frac{n+1}{n}(a_n^2 - H_{n,2}) - 2(a_n - 1), \\ \mathbb{E}[(T - \tau)^2] &= 4\left(\frac{n+1}{n}H_{n,2} + \frac{1}{n-1}\right) - \frac{8a_n}{n-1} + \frac{2}{n(n-1)}(a_n^2 + H_{n,2}), \end{aligned}$$

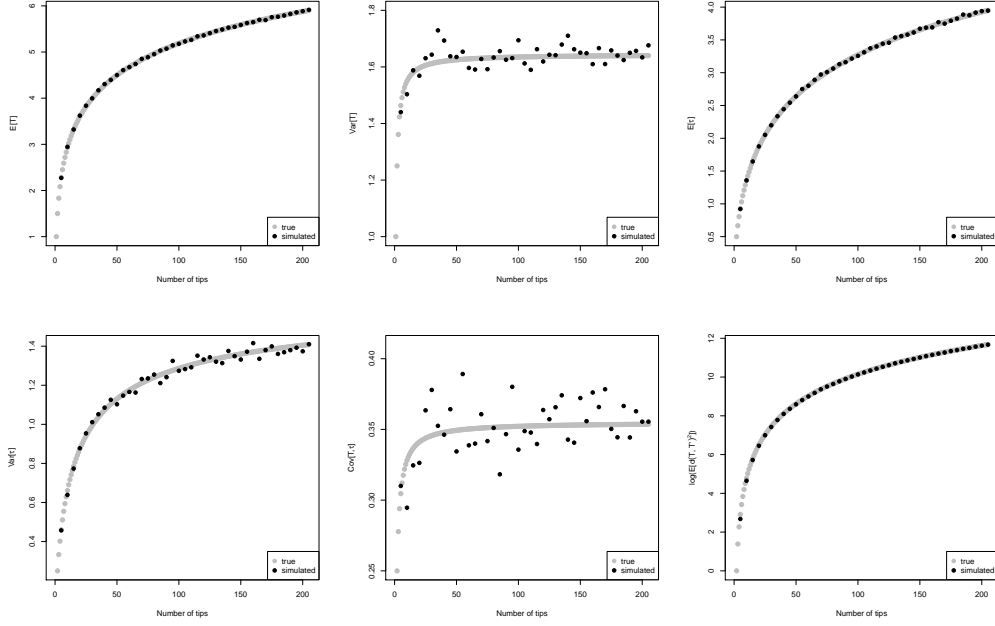


Figure 7: Simulated and true values of $E[T]$ top left, $\text{Var}[T]$ top center, $E[\tau]$ top right, $\text{Var}[\tau]$ bottom left, $\text{Cov}[T, \tau]$ bottom centre, $\log(E[d(\text{Tree}', \text{Tree}'')^2])$ bottom right. Each point comes from 10000 simulated Yule trees.

where $H_{n,2} = \sum_{i=1}^n \frac{1}{i^2}$ is the generalized harmonic number of order 2. The results of this section are illustrated on Fig. 7. Applying directly verifiable identities

$$\sum_{k=1}^{n-1} \frac{a_k}{(k+1)(k+2)} = \frac{n - a_n}{n+1} \rightarrow 1,$$

$$\sum_{k=1}^{n-1} \frac{a_k^2}{(k+1)(k+2)} = H_{n,2} + 1 - \frac{(a_n + 1)^2}{n+1} \rightarrow \frac{\pi^2}{6} + 1,$$

we get the following asymptotic behaviour as $n \rightarrow \infty$

$$\begin{aligned} E[T] &\sim \ln n, & E[\tau] &\sim \ln n, & E[T - \tau] &\rightarrow 2, \\ E[T^2] &\sim \ln^2 n, & E[\tau^2] &\sim \ln^2 n, & E[T\tau] &\sim \ln^2 n, & E[(T - \tau)^2] &\rightarrow \frac{2\pi^2}{3}. \end{aligned}$$

Using the first two moments we get,

$$\begin{aligned}\text{Var}[T] &= H_{n,2}, \\ \text{Var}[\tau] &= \frac{1}{(n-1)^2} ((n^2-1)H_{n,2} - 2(n+1)a_n^2 + 4(n+1)a_n - 4n), \\ \text{Cov}[T, \tau] &= \frac{1}{n-1} (2n - (n+1)H_{n,2}),\end{aligned}\quad (29)$$

so that as $n \rightarrow \infty$

$$\text{Var}[T] \rightarrow \frac{\pi^2}{6}, \quad \text{Var}[\tau] \rightarrow \frac{\pi^2}{6}, \quad \text{Cov}[T, \tau] \rightarrow 2 - \frac{\pi^2}{6},$$

which gives the limiting relationship $\text{Corr}[T, \tau] \rightarrow \frac{12}{\pi^2} - 1 \approx 0.216$.

As an illustration, we apply the obtained results to derive the expectation of a splitted nodal distance between two independent realizations ($Tree'$, $Tree''$) of the conditioned Yule model tree,

$$\text{E}[d(Tree', Tree'')^2] = \frac{2n}{n-1} ((n^2-1)H_{n,2} - 2(n+1)(a_n^2 - 2a_n) - 4n). \quad (30)$$

Given two trees, each with n labelled tips, the function

$$d(Tree', Tree'') = \sqrt{2 \sum_{1 \leq i < j \leq n} (\tau'_{ij} - \tau''_{ij})^2} \quad (31)$$

where τ_{ij} is the height of the most recent common ancestor of tips i and j in the appropriate ultrametric tree, defines a metric on the space of weighted phylogenetic trees (Cardona et al., 2010). Eq. (31) is the weighted-tree counterpart of the path-difference metric (see Steel and Penny, 1993; Cardona et al., 2010; Mir and Rosselló, 2010; Mir et al., 2012)

$$\hat{d}(Tree', Tree'') = \sqrt{\sum_{1 \leq i < j \leq n} (l'_{ij} - l''_{ij})^2},$$

where l'_{ij} , l''_{ij} are the number of speciation events on the path connecting tip nodes i and j in the appropriate tree.

To prove Eq. (30) it is enough to notice that according to Eq. (31) we can write

$$\text{E}[d(Tree', Tree'')^2] = 2 \binom{n}{2} \text{E}[(\tau' - \tau'')^2],$$

where τ' and τ'' are two independent versions of the random variable τ . Since

$$\mathbb{E}[(\tau' - \tau'')^2] = 2 \text{Var}[\tau],$$

Eq. (30) follows from Eq. (29). Note also that Eq. (30) yields as $n \rightarrow \infty$

$$\mathbb{E}[d(\text{Tree}', \text{Tree}'')^2] \sim \frac{\pi^2}{3} n^2.$$

7 All moments of T and τ

Eq. (22) for the Laplace transforms of the random variable T can be used to calculate the moments of T using

$$\mathbb{E}[T^m] = (-1)^m (\partial^m \mathbb{E}[e^{-xT}] / \partial x^m)|_{x=0}. \quad (32)$$

For a fixed n we introduce the following notation

$$\begin{aligned} A(x) &= \frac{1}{x+1} \cdot \dots \cdot \frac{1}{x+n}, \\ b_m(x) &= \frac{1}{(x+1)^m} + \dots + \frac{1}{(x+n)^m}, \\ \mathbf{b}_m(x) &= (b_1(x), \dots, b_m(x)). \end{aligned}$$

Notice that $A(0) = 1/n!$ and $b_m(0) = H_{n,m}$ is the n -th generalized harmonic number of order m

$$H_{n,m} = \sum_{i=1}^n \frac{1}{i^m}. \quad (33)$$

We can write Eq. (22) as $\mathbb{E}[e^{-xT}] = n!A(x)$. Its first derivative with respect to x is $-n!A(x)b_1(x)$, and the second derivative is $n!A(x)(b_1(x)^2 + b_2(x))$. For the general recursive formula we introduce the following notation. We will denote by $\mathbf{k} = (k_1, k_2, \dots)$ infinite dimensional vectors with integer-valued components, and write $\mathbf{k} \in \mathcal{A}_m$ if all $k_i \geq 0$ and $|\mathbf{k}| := \sum_{i=1}^m k_i i = m$. Therefore \mathcal{A}_m represents the set of all possible ways to represent m as a sum of positive integers. We will also use the multi-index notation $\mathbf{b}_m(x)^{\mathbf{k}} = b_1(x)^{k_1} \cdot \dots \cdot b_m(x)^{k_m}$.

Since $A'(x) = -A(x)b_1(x)$, and $b'_m(x) = -mb_{m+1}(x)$, we can show by induction that,

$$\frac{\partial^m}{\partial x^m} \mathbb{E}[e^{-xT}] = (-1)^m n! A(x) \sum_{\mathbf{k} \in \mathcal{A}_m} c_{\mathbf{k}} \mathbf{b}_m(x)^{\mathbf{k}}, \quad (34)$$

where coefficients $c_{\mathbf{k}}$ are defined for all vectors $\mathbf{k} = (k_1, k_2, \dots)$ with integer-valued components using the recursion

$$c_{\mathbf{k}} = \sum_{j=0}^m (jk_j + 1) c_{\mathbf{k}, j}, \quad (35)$$

with $m = |\mathbf{k}|$ and

$$\begin{aligned} c_{\mathbf{k}, 0} &= c_{(k_1-1, k_2, k_3, \dots)}, \\ c_{\mathbf{k}, j} &= c_{(k_1, \dots, k_j+1, k_{j+1}-1, \dots)}, \quad j \geq 1. \end{aligned}$$

The boundary conditions for the recursion of Eq. (35) consist of two parts:

- $c_{\mathbf{k}} = 0$, if all $k_i = 0$, or one of the coordinates of the vector \mathbf{k} is negative,
- $c_{\mathbf{k}} = 1$ if $k_1 \geq 1$ and all other $k_i = 0$.

We conclude from Eq. (34) that

$$\mathbb{E}[T^m] = \sum_{\mathbf{k} \in \mathcal{A}_m} c_{\mathbf{k}} \prod_{i=1}^m H_{n,i}^{k_i}.$$

The technique for calculating the m -th derivative of the Laplace transform of τ given by Eq. (23) is the same but requires new notation

$$\begin{aligned} \hat{A}(y) &= \frac{1}{y-1} \cdot \frac{1}{y+2} \cdot \dots \cdot \frac{1}{y+n}, \\ \hat{b}_m(y) &= \frac{1}{(y-1)^m} + \frac{1}{(y+2)^m} + \dots + \frac{1}{(y+n)^m}. \end{aligned}$$

Notice that $\hat{A}'(y) = -\hat{A}(y)\hat{b}_1(y)$, $\hat{b}'_m(y) = -m\hat{b}_{m+1}(y)$, $\hat{A}(0) = -n!$ and $\hat{b}_m(0) = H_{n,m}$ if m is even or $\hat{b}_m(0) = H_{n,m} - 2$ if m is odd. One can then inductively show that,

$$\begin{aligned} \frac{\partial^m}{\partial y^m} \mathbb{E}[e^{-y\tau}] &= \frac{(-1)^m 2m!}{(n-1)(y-1)^{m-1}} - \frac{(-1)^{m+1}(n+1)!}{n-1} \hat{A}(y)(\hat{b}_1(y))^m \\ &\quad + \sum_{\substack{\mathbf{k} \in \mathcal{A}_m \\ k_1 < m}} c_{\mathbf{k}} \hat{\mathbf{b}}_m(y)^{\mathbf{k}}, \end{aligned}$$

with the coefficients $c_{\mathbf{k}}$ defined as previously by Eq. (35). Therefore, we get

$$\mathbb{E}[\tau^m] = \frac{2m!}{n-1} - (a_n - 2)^m + \sum_{\substack{\mathbf{k} \in \mathcal{A}_m \\ k_1 < m}} c_{\mathbf{k}} \prod_{\substack{i=1 \\ i \text{ odd}}}^m (H_{n,i} - 2)^{k_i} \prod_{\substack{i=1 \\ i \text{ even}}}^m H_{n,i}^{k_i}.$$

Similarly we can use Eq. (27) to calculate the joint moments for $T - \tau$ and τ in terms of

$$A^{(i,j)}(x) = \frac{1}{x+i+1} \cdots \frac{1}{x+j},$$

$$b_m^{(i,j)}(x) = \frac{1}{(x+i+1)^m} + \cdots + \frac{1}{(x+j)^m}.$$

For $m \geq 1$ and $r \geq 1$ we first get

$$\begin{aligned} \frac{\partial^{m+r}}{\partial x^m \partial y^r} \mathbb{E} \left[e^{-x(T-\tau)-y\tau} \right] &= (-1)^{m+r} \frac{2(n+1)!}{n-1} \\ &\times \sum_{j=1}^{n-1} \frac{A^{(0,j)}(x) A^{(j,n)}(y)}{(j+1)(j+2)} \left(\sum_{\mathbf{k} \in \mathcal{A}_m} c_{\mathbf{k}} \mathbf{b}_m^{(0,j)}(x)^{\mathbf{k}} \right) \left(\sum_{\mathbf{k} \in \mathcal{A}_r} c_{\mathbf{k}} \mathbf{b}_r^{(j,n)}(y)^{\mathbf{k}} \right), \end{aligned}$$

and then from the above

$$\begin{aligned} \mathbb{E}[(T - \tau)^m \tau^r] &= (-1)^{m+r} \frac{2(n+1)!}{n-1} \\ &\times \sum_{j=1}^{n-1} \frac{1}{(j+1)(j+2)} \left(\sum_{\mathbf{k} \in \mathcal{A}_m} c_{\mathbf{k}} \prod_{i=1}^m H_{j,i}^{k_i} \right) \left(\sum_{\mathbf{k} \in \mathcal{A}_r} c_{\mathbf{k}} \prod_{i=1}^r (H_{n,i} - H_{j,i})^{k_i} \right). \end{aligned}$$

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